

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte KARL-HEINZ, GERTUND and
GERTUND EBERLE-ADAMKIEWICS

Appeal No. 2001-0756
Application No. 08/666,400

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the
examiner's final rejection of claims 58-67, which are all the claims pending in the
application.

Claim 58 is illustrative of the subject matter on appeal and is reproduced
below:

58. A method for immobilizing biomolecules and affinity ligands, said
method comprising the steps of:
- a) reacting water insoluble matrices, having amino groups and
being selected from the group consisting of test tubes, microtiter
plates, microscope slides, beads, membranes, resins, and
filters, with a cyclobutene carboxylic acid derivative, selected
from the group consisting of cyclobutene carboxylic acid diester,
cyclobutene carboxylic acid halide, cyclobutene carboxylic acid
ester halide, cyclobutene carboxylic acid dialkoxyester, and
cyclobutene carboxylic acid imidazole, as an activating

- compound in methanol in the presence of triethylamine to form active matrices with active groups;
- b) dissolving a protein containing at least one primary or secondary amino group and adding the protein to the activated matrices;
 - c) incubating the activated matrices and the protein of step b) at a pH of 7-10 and a temperature of +4°C to +60°C in an aqueous buffer system, free of primary and secondary amines, to thereby immobilize the protein of step b) on the matrices.

The references relied upon by the examiner are:

Arnold	4,560,504	Dec. 24, 1985
Lau	4,952,519	Aug. 28, 1990

Cuatrecasas et al. (Cuatrecasas), Affinity Chromatography, in Methods in Enzymology, Vol. XXII, pp. 345-378 (William B. Jakoby ed., Academic Press) (1971)

(Harlow), ANTIBODIES, A Laboratory Manual, pp. 522-32, and 528 (Ed Harlow et al., eds., Cold Spring Harbor Laboratory) (1988)

Glüsenkamp et al., "Squaric Acid Diethylester: A Simple and Convenient Coupling Reagent," J. Biosciences, Vol. 46, pp. 498-501 (1991)

Tietze et al. (Tietze), "Squaric Acid Diethyl Ester: A New Coupling Reagent for the Formation of Drug Polymer Conjugates. Synthesis of Squaric Acid Ester Amides and Diamides," Chem. Ber., Vol. 124, No. 5, pp 1215-21 (1991)

GROUND OF REJECTION

Claims 58-67 stand rejected under 35 U.S.C. § 103 as being unpatentable over Tietze or Glüsenkamp in view of Harlow, Arnold, Cuatrecasas and Lau.

We reverse.

DISCUSSION

The examiner relies (Answer, page 5) on Tietze and Glüsenkamp in the alternative to "teach the use of a cyclobutane carboxylic acid derivative to conjugate amine bearing molecules conducting the reaction in either inert solvents (viz, ethanol) or non-amine containing aqueous buffers at pH7."

According to the examiner (id.) neither reference teaches “a post coupling reaction to quench ... the unreacted coupling reagent.” Therefore, the examiner relies on Harlow to “teach a post coupling reaction to quench unreacted coupling reagent.” Id. The examiner relies on Arnold, Cuatrecasas and Lau to teach various aminated supports including glass, cellulose, agarose beads, polystyrene and polypropylene. Answer, pages 6-7.

We note that none of the references relied on by the examiner teach the use of methanol in the presence of triethylamine as is required in step A of appellants’ claimed invention. In order to make up this deficiency, the examiner asserts (Answer, page 6), “the use of ethanol/triethylamine [as taught by both Tietze and Glösenkamp] for the reaction of squaric acid with amine containing compounds ... renders obvious the use of methanol/triethyl-amine for the reaction of squaric acid with amines.”

The examiner, however, provides no evidence to support his assertion. In this regard we note that “[i]t is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teachings of the prior art so that the claimed invention is rendered obvious.” In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992), citing In re Gorman, 933 F.2d 982, 987, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). Rather, the examiner may establish a case of prima facie obviousness based on a combination of references “only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” Id., 972 F.2d at

1265, 23 USPQ2d at 1783. “The factual inquiry whether to combine references must be thorough and searching.” In re Lee, 277 F.3d 1338, 1343, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002), quoting McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001).

Moreover, it is improper for this board, and for that matter the examiner, to hold claims upatentable for obviousness based solely on conclusory statements about what is “common knowledge” or “well known” in the art, without objective evidence in support of that knowledge. See Lee, 277 F.3d at 1344, 61 USPQ2d at 1434-1435. On this record, there is no evidence directing a person of ordinary skill in the art to the use of methanol instead of ethanol as is required in step A of the claimed invention.

Since the examiner failed to establish a factual basis in the evidence to support his conclusion that the teaching of ethanol/triethylamine renders obvious the use of methanol/triethyl-amine for the reaction of squaric acid with amines we are compelled to reverse the rejection of record.

Accordingly we are compelled to reverse the rejection of claims 58-67
under 35 U.S.C. § 103.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
)	
)	
)	BOARD OF PATENT
Toni R. Scheiner)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
)	
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